Rejections under 35 U.S.C. 112, 2nd Paragraph

Claims 1-11 stand rejected under 35 U.S.C. §112, second paragraph. Applicants have amended claim 1 to relate back to the preamble, as suggested in the Office Action of December 13, 2002, at page 2.

Claim 7 also stands rejected under 35 U.S.C. 112, second paragraph as indefinite for not referring to specific hybridization conditions. Applicants note that claim 7 has been amended to eliminate any reference to hybridization. Applicants assert that claim 7 as amended, when combined with the limitations of the parent claim 1, is not indefinite, because the skilled artisan could readily determine the metes and bounds of the claim.

Based on the claim amendments and the above discussion, applicants respectfully request reconsideration and withdrawal of the rejections under 35 U.S.C. 112, second paragraph.

Rejections under 35 U.S.C. 102(b)

Claims 1, 2, 10, and 11 stand rejected under 35 U.S.C. 102(b), as being anticipated by Cancroft et al. (1973), as evidenced by Socolow et al. (1967), Tazebay et al. (2000), and Spitzweg et al. (1998). It is asserted that the method described in Cancroft et al. inherently comprises the same method steps as claimed in the instant invention, although Cancroft et al. was not aware of the mechanism utilized.

Applicants respectfully request reconsideration and withdrawal of these rejections based on the claim amendments and the following discussion.

Applicants note that claim 10 and 11 have been cancelled, and claim 1 has been amended to incorporate the limitation of claim 3 that the agent specifically and selectively binds to mgNIS. Since (cancelled) claim 3 was not held to be anticipated by Cancroft et al, and claim 1 and dependent claim 2 incorporates the claim 3 limitation, applicants assert that claims 1 and 2 cannot be anticipated by Cancroft et al. Accordingly, withdrawal of the rejection under 35 U.S.C. 102(b) is requested.

Accordingly, withdrawal of the rejection under 35 U.S.C. 102(b) is requested.

Rejections under 35 U.S.C. 103(a)

Claims 1-11 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Cancroft et al. (1973), in view of Eskin et al. (1974), Spitzweg et al. (1998), and Jhiang et al. (1998). In a rejection maintained from the previous Office Action, it is asserted that (a) Cancroft et al. teaches a method for diagnosing breast cancer using ^{99m}Tc-pertechnetate but does not teach that ^{99m}Tc-pertechnetate is concentrated in malignant breast masses. However, it is asserted that the ^{99m}Tc-pertechnetate concentration is taught by Socolow et al. and Spitzweg et al. and thus the ^{99m}Tc-pertechnetate reflects the level of expression of mgNIS. Additionally, Cancroft et al does not teach that expression of mgNIS can be measured by radioiodide. However, it is further asserted that Eskin et al. teach that radiolabeled iodide concentration is higher in breast tissue with carcinoma or dysplasia, and Spitzweg et al. teach that the ability of thyroid tissue to selectively concentrate radioiodide is dependent on NIS activity, and Jhiang et al. teach immunohistochemical analysis of human NIS in tissue. It is thus asserted that it would be obvious to identify the presence of breast tissue that expresses higher levels of mgNIS by the method of Jhang et al. of Spitzweg et al. because Cancroft et al. and Eskin et al. teaches higher amounts of ^{99m}Tc-pertechnetate and radioiodide, respectively, is diagnostic of breast cancer, and that the use of the antibody of Jhiang et al. can be used as a modification of the method of Cancroft et al. to confirm the diagnosis of breast cancer.

Applicants respectfully request reconsideration and withdrawal of this rejection for the following reasons.

In Cancroft, only 6 patients were evaluated. All were "selected from those referred for mammography" for existing breast masses (Cancroft et al, page 441). There was no analysis of patients that were not known to have breast cancer, nor was there any blind study of whether a patient with breast cancer could be distinguished from a patient that did not have breast cancer. Indeed, Cancroft et al. recognized that Their

method was not for diagnosing breast cancer, since they concluded that there was "good correlation between physical examination, mammography, and radionuclide breast imaging", and suggested that "(t)he method described here may be useful as a supplemental approach" (Cancroft et al. at page 444).

A skilled artisan, on reading Cancroft et al., would thus conclude that the method described was not useful as a means of primary diagnosis but rather a supplement to standard diagnostic techniques such as physical examination and mammography. Cancroft et al. thus merely suggests a method of providing confirmatory evidence of the presence of breast cancer in those cases already identified by standard diagnostic techniques.

Other references cited by the Examiner teach away from the claimed method of using an agent that specifically and selectively binds to mgNIS for the diagnosis of breast cancer.

For example, Kilbane et al. teaches that the "expression of the NIS was found to be a feature of both fibroadenomata and breast carcinoma tissue" (Kilbane et al., page 6). This would indicate to a skilled artisan that benign breast tissue (fibroadenomata) can also overexpresses mgNIS. A similar conclusion may be reached from the results obtained by Eskin et al. who noted that "the ^{131}I concentration in breast tissue with carcinoma or dysplasia was higher than that in histologically normal tissues." Eskin et al., page 398. Thus, Eskin et al., like Kilbane et al. also notes the potential for higher concentration of radioiodide in noncancerous tissue (dysplasia).

Based on the above, applicants assert that the prima facie case for obviousness cannot be maintained because the combination of references does not teach or suggest every limitation of the claims. This is because there is no teaching or suggestion that mgNIS detection can be used as "a method for detecting the presence or absence of breast cancer" as claimed, because Cancroft et al. only teaches a confirmatory role for the method disclosed therein and did not look at patients that were not known to have breast cancer, and none of the other references teach or suggest that detection of

mgNIS, either by direct detection or by detecting the result of mgNIS presence (accumulation of ^{99m}Tc-pertechnetate or radioiodide), could be used for detecting (vs. confirming) breast cancer.

Additionally, the cited art actually teaches away from the claimed method because the combination of references teach that non-cancerous breast tissue can also express mgNIS. The skilled artisan would thus not know how extensive this expression in non-cancerous tissue would be. The cited combination of references would therefore not provide the skilled artisan with a reasonable expectation of success for practicing the claimed invention, particularly with respect to the limitation that the expression of mgNIS is indicative of the presence of breast cancer. Accordingly, reconsideration and withdrawal of the rejection is respectfully requested.

Conclusions

In light of the claim amendments and the above discussion, applicants respectfully request reconsideration and withdrawal of all rejections and passage of the pending claims namely claims 1, 2, 4-9 and 29, to allowance. If there are any minor issues that would prevent allowance of the claims, applicants request that the Examiner contact the undersigned attorney.

Respectfully submitted,

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Dated: New York, New York
April 12, 2002

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~~Marked Up Claims~~ as Amended in Reply of April 12, 2002
U.S. Patent Application 09/519,959
Additions are underlined and deletions are bracketed

1. (amended) A method for [diagnosing]detecting the presence or absence of breast cancer in a non-lactating subject, comprising determining whether or not mammary gland sodium/iodide symporter (mgNIS) is expressed in breast tissue of the subject using an agent that specifically and selectively binds to mgNIS, wherein [detection of]expression of mgNIS in the breast tissue is indicative of the presence of breast cancer in the subject, and no [detection of]expression of mgNIS in the breast tissue is indicative of the absence of breast cancer in the subject.

2. The method of Claim 1, wherein the expression of mgNIS is detected *in vitro* or *in vivo*.

4. The method of Claim 3, wherein the agent is labeled with a detectable marker.

5. The method of Claim 3, wherein the agent is an antibody.

6. The method of Claim 5, wherein the antibody is labeled with a detectable marker.

7. (amended) The method of claim 1, wherein the expression of mgNIS is detected using at least one nucleic acid probe[that specifically and selectively hybridizes to nucleic acid encoding mgNIS].

8. (Amended) The method of claim 7, wherein the nucleic acid probe is DNA[or RNA].

9. The method of Claim 7, wherein the nucleic acid probe is labeled with a detectable marker.

29. (New) The method of claim 7, wherein the nucleic acid probe is RNA.